

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : Holmaas *et al.*
Application No. : 10/560,497
Filing Date : December 12, 2005
Art Unit : 1621
Title : Process for Iohexol Manufacture

Docket No. : PN0324

Mail Stop Reply Brief – Patents
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REPLY BRIEF

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I. STATUS OF CLAIMS

Claims 1-21 are pending in this application. The Examiner has rejected all of these claims. Appellants are appealing the rejections of Claims 1-21.

II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues for review in this appeal arise from an Examiner's Answer that was mailed on May 27, 2009.

The Examiner rejected claims 1-21 under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,948,940 to Malthe-Sorensen et al. ("Malthe-Sorensen").

III. ARGUMENT

Appellants respectfully point out here that they are only addressing the Examiner's Answer ("Answer") dated May 27, 2009 herein. Please see Appellants Appeal Brief dated April 3, 2009 for a complete Responsive Brief.

Appellants respectfully request that The Board of Patent Appeals and Interferences ("Board") should reverse the Examiner's rejection based on the Examiner's Answer for the reasons set forth below.

On page 5 of the Examiner's Response to Appellants, the Examiner states that he "contends that Malthe-Sorensen clearly suggested to one having ordinary skill in the art the use

of similar solvents.” Appellants submit that Malthe-Sorensen describes a process for the production of iohexol where the solvent used is 2-methoxy-ethanol. Malthe-Sorensen does not teach, describe, or suggest using any other solvent other than 2-methoxy-ethanol. There are no indications in Malthe-Sorensen regarding which solvent might be used as an alternative solvent and there are not even indications that alternative solvents could be used. Accordingly, Malthe-Sorensen clearly suggests the use of 2-methoxy-ethanol and no other alternatives.

The fact that Malthe-Sorensen does not speak in general of solvents, but only of 2-methoxy-ethanol specifically, clearly does not imply “suggesting the use of similar solvents”, rather to the contrary. Appellants wish to remind the Examiner that “the prior art itself must provide a motivation or reason for the worker in the art, without the benefit of the Applicant’s specification, to make necessary changes in the reference device”. See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984).

In addition to the subject matter described in Malthe-Sorensen it was known from WO02/083623, as discussed in the present specification, page 2, lines 1-2, to use 1-methoxy-2-propanol as solvent in the purification by recrystallization of iohexol.

The fact that a solvent is known for its use as the dominant solvent in the crystallisation step of the same process would clearly teach away from using the same in the alkylation step. ‘Teaching away’ simply means teaching a solution that would not lead to the claimed subject matter. As noted by the Federal Circuit:

A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

Para-Ordinance Mfg. v. SGS Importers Int'l, 73 F.3d 1085 (Fed. Cir. 1995).

Knowing that 1-methoxy-2-propanol is used as the solvent in the purification by recrystallization of iohexol, one skilled in the art would not expect that the same solvent could also be used in the alkylation step. The reason for this is that in the alkylation step it is required that the solvent shows good solubility for 5-(acetamido)-N,N'bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide and that the product (iohexol) does not precipitate during the reaction, whereas in the purification step the solvent used should show little solubility for the product (iohexol). A person skilled in the art would therefore not expect that 1-methoxy-2-propanol could successfully be used as solvent in both the alkylation and the purification step, and would not think or suggest using 1-methoxy-2-propanol as an alternative to 2-methoxy-ethanol in the production described by Malthe-Sorensen. Malthe-Sorensen does describe using 2-methoxy-ethanol as a solvent in both the alkylation and in the purification step, however, the solvent mixture only comprises a very small amount of 2-methoxy-ethanol in the purification step, see claim 1.

In addition to the arguments discussed above other aspects supported the belief that 1-methoxy-2-propanol could not be used as solvent in the current process, thereby making it unobvious to try. In short, 2-ethoxyethanol was considered as an alternative solvent but was found to have too poor solubility. Knowing that 1-methoxy-2-propanol was even less polar there were no reason to pursue 1-methoxy-2-propanol as solvent. In addition, one could consider

adding co-solvents to improve solubility, but knowing that such addition to 2-methoxy-ethanol used in the current process worsen the selectivity only supported the belief that 1-methoxy-2-propanol could not be used.

Additionally, to expect one skilled in the art reading Malthe-Sorensen to try 1-methoxy-2-propanol as an alternative solvent would clearly involve using hindsight. The skilled artisan would have to:

1. Attempt to use alternative solvents even though Malthe-Sorensen specifically concerns the use of 2-methoxy-ethanol and in no way suggests that other solvents might work;
2. Discover that 1-methoxy-2-propanol is an alternative solvent among a vast number of compounds; and
3. Disregard the known facts indicating that 1-methoxy-2-propanol would not work as a solvent in the alkylation step.

Appellants therefore respectfully request that the Board should reverse the Examiner's obviousness rejection of claims 1-21 since Malthe-Sorensen Fail to Disclose, Teach or Suggest All the Elements of Claims 1-21.

IV. CONCLUSION

In view of the foregoing, Appellants respectfully request that the Board reverse the rejections of Claims 1-21 as set forth in the Examiner's Amendment mailed May 27, 2009, that the Board allow the pending claims since they are in condition for allowance, and that the Board grant any other relief as it deems proper.

Dated: July 27, 2009

Respectfully submitted,

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